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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/858,332	05/15/2001	Grigoriy S. Tchaga	CLON-056CIP	2176
41064	7590	05/19/2004	EXAMINER	
BOZICEVIC, FIELD & FRANCIS (BD BIOSCIENCES) 200 MIDDLEFIELD ROAD, SUITE 200 MENLO PARK, CA 94025			KERR, KATHLEEN M	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/858,332	Applicant(s) TCHAGA ET AL.	
	Examiner Kathleen M Kerr	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-20 and 26-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-20 and 26-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-final rejection (mailed on November 4, 2003), Applicants filed a response and amendment received on March 3, 2004. Said amendment cancelled Claims 1-14 and 21-25, amended Claims 15 and 16, and added new Claims 29-38. Thus, Claims 15-20 and 26-38 are pending and will be examined herein.

Priority

2. The instant application is granted the benefit of priority for the U.S. Application Nos. 60/101,867 and 09/404,017 filed on September 25, 1998 and September 23, 1999, respectively, as requested in the first lines of the specification. The Examiner notes, however, that no disclosure of the genus of Claims 15-20 and 26-28 is found in either priority application; disclosure of Claim 29 (n=6) and Claim 30 is found in 60/101,867, Figure 3. Thus, Claims 15-20 and 26-28 are afforded an earliest effective filing date of May 15, 2001, the filing date of the instant application; and Claims 29-38 are afforded an earliest effective filing date of September 25, 1998.

Compliance with the Sequence Rules

3. In response to the previous Office action, Applicant filed a new sequence listing in computer readable form and paper copy containing 23 sequences. Said sequence listing has been entered.

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4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

a) In paragraph 20, a 5-mer polypeptide is disclosed without benefit of SEQ ID NO.

The noted sequences are not in the sequence listing as filed, thus Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO. See also below objections for inconsistencies with the sequence listing that will also need amendment.

Withdrawn - Objections to the Specification

5. Previous objection to the specification because the title is not descriptive is withdrawn by virtue of Applicant's amendment to the title.

Maintained - Objections to the Specification

6. Previous objection to the Abstract is maintained. The Abstract should be a single paragraph and the inclusion of the claim-like indentation is confusing and cannot be repeated in print. Applicant is requested to set forth the Abstract as a single paragraph (see M.P.E.P. § 608.01(b)).

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New - Objections to the Specification

7. The specification is objected to for the following inconsistencies between the sequence listing and the disclosure:

- a) In Figure 2, specifically Figure 2B, a polypeptide in addition to SEQ ID NO:14 as described in the Brief Description of the Drawings, is disclosed (see line 1921/641-2100/700); this sequence must be given a SEQ ID NO and mentioned in the Brief Description or must be deleted from the drawing (its inclusion is confusing).
Also, the DNA of Figure 2 (3426 base pairs long) is described as SEQ ID NO:13 in the Brief Description; however, SEQ ID NO:13 in the sequence listing is 3430 base pairs long.
- b) In Figure 3, the DNA of insert 3 is described as SEQ ID NO:28 (see amendment faxed in on September 11, 2003, originally submitted on or about April 8, 2003); this must be a typographical error because no SEQ ID NO:28 is in the sequence listing. Perhaps the sequence is SEQ ID NO:18.
Also in Figure 3, the protein of insert 4 is an 18-mer of (His-Glu-Glu)₆ described in the Brief Description as SEQ ID NO:3 (see amendment faxed in on September 11, 2003, originally submitted on or about April 8, 2003). This same sequence, (His-Glu-Glu)₆, is in paragraph [0063] as SEQ ID NO:3. However, SEQ ID NO:3 is a 16-mer, apparently missing the final two Glu residues.
Also in Figure 3, the protein of insert 5 is described in the Brief Description as SEQ ID NO:4 (see amendment faxed in on September 11, 2003, originally submitted on or about April 8, 2003). However, SEQ ID NO:4 is (His-Asp-Glu)₆ and insert 5 is (His-Asp-Glu)₂-(His-Glu-Asn)₂-(His-Glu-Asp)₂. No SEQ ID NO describing insert 5 is found in the sequence listing at present.
- c) In paragraphs [0068] and [0069], all the sequences are described in error as amended by Applicant on December 10, 2002:
(Asp)₄Lys, called SEQ ID NO:6, is not found in the sequence listing,
Ile-Glu-Gly-Arg, called SEQ ID NO:7, is SEQ ID NO:6 in the present sequence listing,
Leu-Val-Pro-Arg-Gly-Ser, called SEQ ID NO:8, is SEQ ID NO:7 in the sequence listing, and
His-Pro-Phe-His-Leu-Val-Ile-His, called SEQ ID NO:9, is SEQ ID NO:8 in the sequence listing.
The three tags in paragraph [0069] are described as SEQ ID NOs: 10-12, respectively, but in the sequence listing of record they are SEQ ID NOs: 9-11, respectively.
- d) SEQ ID NO:11 = SEQ ID NO:12 in the sequence listing (it is a duplicate).

Careful consideration and correction of the sequence listing and the description of sequences in the specification is required. The Examiner also notes the above issue of paragraph [0020] containing a sequence without a SEQ ID NO so when amending the sequence listing to correct the above errors, the sequence from paragraph [0020] should also be included.

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8. The specification is objected to for having a confusing reference. In paragraph [0102], the reference to “U.S. RE 30,985” is unclear. Clarification is required.

Withdrawn - Claim Objections

9. Previous objection to Claim 15 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicant’s amendment to Claim 15.

10. Previous objection of Claims 15-20 and 26-28 for depending from non-elected claims is withdrawn by virtue of Applicant’s amendment of Claim 15 to an independent claim.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

11. Previous rejection of Claims 15-20 and 26-28 under 35 U.S.C. § 112, second paragraph, as being indefinite for the makeup of the side chains in formulas 1 and 3 is withdrawn by virtue of Applicant’s amendment to only formulas with exact amino acid compositions.

Maintained - Claim Rejections - 35 U.S.C. § 112

12. Previous rejection of Claim 16 under 35 U.S.C. § 112, second paragraph, is maintained. Moreover, new Claim 31 is added to the instant rejection. Thus, Claims 16 and 31 are rejected under 35 U.S.C. § 112, second paragraph. Applicant’s arguments have been fully considered but are not deemed persuasive. Applicant argues that it is clear from the claim language that metal affinity peptide must be fused to amino or carboxy terminal residue; the Examiner disagrees. The open claim language of Claims 16 and 31 (“the polynucleotide **comprises**” and “a fusion protein **comprising** a polyketide”) allows for protein or polynucleotide sequence attached to

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what is exactly described in the claims. Thus, the metal affinity sequence can be embedded in a polypeptide so long as polypeptide is on at least one side of the affinity sequence. Therefore, the implication of something at the termini of the polypeptide is confusing as previously noted by the Examiner. Clarification is required.

New - Claim Rejections - 35 U.S.C. § 112

13. Claims 15-20 and 26-28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 15, the inclusion of SEQ ID NO:22 is confusing because SEQ ID NO:22 is exactly $n=3$. The Examiner suggests moving the parentheses to after “ $n=3$ ” for clarity.

14. Claims 30-38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 30, the use of “ NH_2 -” and “- COOH ” in the description of the sequence is confusing. Firstly, Claims 30 and 32-38 are wholly open language and the specification describes the use of the affinity tag polypeptide in a fusion protein; however, reciting both an N-terminus and a C-terminus on the tag polypeptide appears to close the claim language to “consisting of” since no other polypeptide sequence would be attached. Moreover, for Claim 31 the language is wholly confusing since an indication of a fusion protein is noted, albeit unclearly. Clarification is required.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

15. Claims 15-20 and 26-38 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Claims 15 and 30, as written, do not sufficiently distinguish over polynucleotides as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of “isolated” or “purified” provided that support in the specification can be cited. See M.P.E.P. § 2105.

Withdrawn - Claim Rejections - 35 U.S.C. § 102

16. Previous rejection of Claims 15-19 and 26-28 under 35 U.S.C. § 102(b) as being anticipated by Chaga *et al.* is withdrawn by virtue of Applicant’s removing reference to generic formula 1 in said claims.

17. Previous rejection of Claims 15 and 17-19 under 35 U.S.C. § 102(b) as being anticipated by Giraldo *et al.* is withdrawn by virtue of Applicant’s amendment removing claims to generic formula 3.

Maintained - Claim Rejections - 35 U.S.C. § 102

18. Previous rejection of Claims 15 and 17-20 under 35 U.S.C. § 102(e) as being anticipated by Sato (USPAP 2003/0079237A1 filed June 7, 1999) is maintained. Moreover, the Examiner is adding Claim 16 to the instant rejection due to the lack of clarity of said claim. Thus, Claims 15-20 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Sato. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Applicant argues that Claims 15-20 are full entitled to the claimed priority date of September 25, 1998; the Examiner disagrees. Nowhere in the priority document is the formula of Claim 15 disclosed. A similar sequence wherein $n=6$ is disclosed in Figure 3; however, this disclosure does not support the claimed genus.

As previously noted, "Sato teaches a nucleic acid molecule that encodes mouse p75NTR (NADE); the sequence of mouse NADE comprises an internal fragment: His-Asn-His-Asn-His-Asn (see Figure 1A) that meets the limitations of formula 2. Sato also teaches vectors (see paragraph [0137]) and prokaryotic and eukaryotic host cells (see paragraph [0143]) of the mouse NADE DNA sequence." The Examiner further notes that the internal sequence of (His-Asn)₇ can be considered an amino terminus tag for the downstream sequence and can be considered a carboxy terminus tag for the upstream sequence, thus meeting the limitation of Claim 16.

New - Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

19. Claims 15-19 and 26-28 are rejected under 35 U.S.C. § 102(b) as being anticipated by CLONTECHniques (PROTet™ 6xHN Bacterial Expression System. October, 1999. pages 23-24). The instant claims are drawn to vectors comprising a (His-Asn)₃₋₁₀ affinity tag for a fusion protein, prokaryotic host cells thereof and kits thereof.

CLONTECHniques (Oct, 1999) teach a 6xHN bacterial expression system kit comprising a vector for expressing a (His-Asn)₆ tagged protein in *E. coli*, as well as resin, column, and buffers.

20. Claims 30-33 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hirota *et al.* (see IDS). The instant claims are drawn to vectors comprising SEQ ID NO:1.

Hirota *et al.* teach a polynucleotide comprising SEQ ID NO:1 near its N-terminus; Hirota *et al.* also teach using a cDNA library, which inherently comprises vectors and host cells.

21. Claims 30-34 and 36-38 are rejected under 35 U.S.C. § 102(a) as being anticipated by CLONTECHniques (HAT™ Protein Expression & Purification System. July, 1998). The instant claims are drawn to vectors comprising SEQ ID NO:1 as an affinity tag for a fusion protein, prokaryotic host cells thereof and kits thereof.

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CLONTECHniques (July, 1998) teach a bacterial expression system kit comprising a vector for expressing a HAT-tagged protein, as well as resin, column, and buffers, wherein the HAT sequence comprises SEQ ID NO:1 (see especially Figure 1 legend).

Other References Cited

22. The following reference has been cited previously to complete the record:
- a) Zhang *et al.* USPN 5,670,483 teaches a (His-Asn)_x peptide as an affinity peptide (see Table 2, item HN16, SEQ ID NO:53) but do not teach DNA encoding the peptide; the peptides throughout Zhang *et al.* are made by peptide synthesizers, not for fusion proteins.

Summary of Pending Issues

23. The following is a summary of the issues pending in the instant application:
- a) Compliance with the sequence rules for a sequence found on page 20 of the application.
 - b) The Abstract stands objected to.
 - c) The specification stands objected to for inconsistencies between the sequence listing and the disclosure.
 - d) The specification stands objected to for having a confusing reference.
 - e) Claims 16 and 31 stand rejected under 35 U.S.C. § 112, second paragraph, for the amino- or carboxy-terminal language.
 - f) Claims 15-20 and 26-28 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the inclusion of SEQ ID NO:22.
 - g) Claims 30-38 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the use of "NH₂-" and "-COOH".
 - h) Claims 15-20 and 26-38 stand rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.
 - i) Claims 15 and 17-20 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Sato.
 - j) Claims 15-19 and 26-28 stand rejected under 35 U.S.C. § 102(b) as being anticipated by CLONTECHniques.
 - k) Claims 30-33 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Hirota *et al.* (see IDS).
 - l) Claims 30-34 and 36-38 stand rejected under 35 U.S.C. § 102(a) as being anticipated by CLONTECHniques.

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Conclusion

24. Claims 15-20 and 26-38 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution. Due to new issues raised concerning the sequence listing and the specification, the instant Office action is **NON-FINAL**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kathleen M Kerr
Examiner
Art Unit 1652

May 14, 2004